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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,857	08/27/2002	Richard Guilfoyle	GELOG	2254
23599	7590	05/18/2004	EXAMINER	
MILLEN, WHITE, ZELANO & BRANIGAN, P.C. 2200 CLARENDON BLVD. SUITE 1400 ARLINGTON, VA 22201			LY, CHEYNE D	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/088,857

Applicant(s)

GUILFOYLE, RICHARD

Examiner

Cheyne D Ly

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-38 is/are rejected.
- 7) ☒ Claim(s) 27 and 28 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Applicant's election with traversal of Group II, claims 2, 3, and 5-38, filed March 01, 2004, is acknowledged.
2. The restriction requirement, mailed January 29, 2004, has been withdrawn.
3. It is noted that Applicant has submitted the first page of a PCT published application to be used as an abstract for this instant Application. It is suggested that Applicant submit an abstract commencing on a separate sheet of paper to avoid any future complications in the event that the instant Application is to be issued as a patent. It is further noted that this is not a requirement but a suggestion to avoid future complications that would impede the instant Application from being issued.
4. Claims 1-38 are examined on the merits.

SEQUENCE COMPLIANCE

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). See, for example, Figures 2 and 3. However, this application fails to comply with the requirements of 37 CFR § 1.821 through 1.825 because Figures 2 and 3, contain nucleic acid sequences with sequence lengths that are equal to or greater than 10 nucleic acid molecules and these sequences do not have SEQ ID Nos cited along with each sequence in the specification or Figure. Applicants are also reminded that SEQ ID Nos are not required in Figures per se, however, the corresponding SEQ ID Nos then are required in the Brief Description of the Drawings section in the specification. Applicants are also reminded that a CD-ROM sequence listing submission may replace the paper and computer readable form sequence listing copies. Applicant(s) are

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required to submit a new computer readable form sequence listing, a paper copy for the specification, statements under 37 CFR § 1.821(f) and (g), if there is a need to list additional sequences in the listing. Applicant(s) are given the same response time regarding this failure to comply as that set forth to respond to this office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.

OBJECTIONS

6. The title of the invention is not descriptive because the instant title is directed to “indexing populations” while the claimed invention is directed to a method and a device. A new title is required that is clearly indicative of the invention to which the claims are directed.

7. Claim 28 is objected to because of the following informalities: Claim 28, lines 1 and 2, contains the terms “sequ nce” and “cite” which are misspelled. Specific to the term “cite”, said term is misspelled within the context of the well known in the art phrase “restriction site.”

Appropriate correction is required.

8. Claim 27 is objected to because of the following informalities: Claim 27 ends in a comma which is improper. Appropriate correction is required.

9. The disclosure is objected to because of the following informalities: Page 51, the title under “EXAMPLE 1” has a number of misspelled words wherein said words comprise missing letters. Appropriate correction is required.

CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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11. Claims 5-28, and 30-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Specific to claims 5-20, 22-28, and 30-38, line 1, the term “paragraph” causes the claims to be vague and indefinite because it is unclear as to what “paragraph” represents in regard to the dependency relationship of the respective claims.

13. Specific to claims 21 and 33, line 1, the phrase “to 17” or “to 29” causes the claims to be vague and indefinite because it is unclear as to what “to 17” or “to 29” represents in regard to the dependency relationship of the respective claims. Claims 21 and 33 are unclear because said claims lack the word “claim” before “17” or “29” to indicate that claim 21 or 33 is dependent from the respective claim 17 or 29.

14. Specific to claim 26, line 1; claim 27, steps (A) and (B), Applicant uses the abbreviations of “stand-d”. Abbreviations in claims are vague and indefinite unless accompanied by the full name, usually in parentheses.

15. Claim 27, steps (A) and (B), is vague and indefinite because it is unclear whether steps (A) and (B) are actual steps due to the awkward and fragmented English language construction. For example, the phrase “distributing strand-d is placement indexing adaptors into discrete containers” is unclear because it is unclear what is going into the discrete containers.

CLAIM REJECTIONS - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 1, 8-12, and 17-38 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Guilfoyle et al. (1997).
18. Guilfoyle et al. discloses a method and device (PTC-200 DNA) engine for indexing a population (page 1854, column 1, Abstract etc.) of 65,536 pair-wise combinations of indexing sequences by PCR amplification (product) comprising adaptor and oligomers (reagents) (page 1872, column 1, lines 3-15), as in instant claim 1, lines 1-5.
19. "A simple calculation for 6-cutters predicts that 256 individual...will produce on average 244 fragments" (sequence specific sub-populations) (page 1872, column 1, 16-21) wherein the cited subpopulation is a substantial all fraction, as in instant claims 1, lines 6-7; claims 9-12; claims 22-24; claims 30; claim 31; claim 35; claim 37, and claim 38.
20. The PCR reactions (plurality of containers) occur in 100 ul PCR reaction solution under the same condition (homogenous) and 20 ul of each product is loaded into a 0.8% gel (homogeneous) (page 1871, Figure 1, lines 10-11). The inclusion of a reference by The Scientist (1998) is note being used as prior art but only to show the inherent characteristic of the cited PTC-200 DNA Engine. The scientist discloses the PTC-200 DNA Engine is has the capacity to handle V-bottom 96 well plates (micro-titer plate) (The Scientist, 3rd row, 2nd column), , as in instant claim 1, lines 8-9; claim 29; and claim 32.
21. The method of Guilfoyle et al. comprises individual sequence of λ BclI fragments wherein said fragments are amplified using pairs of known indexing sequence (probes) and primer oligonucleotides (page 1870, column 1, lines 41-46, page 1871, Figure 3), as in instant claims 17, 25, and 33.

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22. The indexing sequence of Guilfoyle et al. comprises of 4 nucleotides wherein the uniqueness is confined to 256 possible 4mers (page 1870, column 1, lines 24-27, and Figure 2), as in instant claims 18-21, 34, and 36.

23. The method of Guilfoyle et al. comprises a strand-displaced structure wherein five nucleotides are displaced via contact with the doubled stranded portion of the target molecule and the indexing sequence of the adaptor is displaced by the restricting fragment (multiplex). The method of Guilfoyle et al. requires amplifying the restriction fragments in a thermal cycler (container), extending the displaced strand from its 3' end, and the invading or displace 4 nt region as the 'indexing sequence' to show individual fragments can be amplified (page 1870, column 1, lines 3-46). Further, the amount of amplified polynucleotide is quantified (Figure 3) for indexing the population of the polynucleotide (page 1872, column 1, lines 32-61), as in instant claims 8, 26, and 27.

24. The method of Guilfoyle et al. is directed to class-II restriction enzymes wherein the restriction site is continuous with a five nucleotide base-pair sequence of the overhanging sequence (page 1854, column 2, lines 4-18), as in instant claim 28.

CLAIM REJECTIONS - 35 USC § 103

25. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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26. Claims 1-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guilfoyle et al. (1997) taken with Vogelstein et al. (August 1999) in combination with Kato (1996).

27. Guilfoyle et al. the limitation to claims 1, 8-12, and 17-38 as discussed above.

28. Further, Guilfoyle et al. discloses a method and device (PTC-200 DNA) engine for indexing a population (page 1854, column 1, Abstract etc.) of 65,536 pair-wise combinations of indexing sequences by PCR amplification (product) comprising adaptor and oligomers (reagents) (page 1872, column 1, lines 3-15), as in instant claim 2-4, lines 1-5.

29. "A simple calculation for 6-cutters predicts that 256 individual...will produce on average 244 fragments" (sequence specific sub-populations) (page 1872, column 1, 16-21) wherein the cited subpopulation is a substantial all fraction, as in instant claims 2-4, lines 6-7.

30. The PCR reactions occur in 100 ul PCR reaction solution under the same condition (homogenous) and 20 ul of each product is loaded into a 0.8% gel (homogeneous) (page 1871, Figure 1, lines 10-11), as in instant claim 3, line 8; and claim 4, lines 8-9.

31. However, Guilfoyle et al. does not disclose of claims 2-7 and 13-16.

32. Vogelstein et al. discloses an improvement for quantifying PCR products wherein the PCR products are in homogenous media (page 9236, column 1, line 22, to column 2, line 7).

The method of Vogelstein et al. comprises measuring fluorescence intensity (kinetic data) of PCR products in a plate directly from the reaction incubation period of 10-60 (continuous) minutes without a step of physically separating determined products from the reactions (Vogelstein et al., pages 9236-9237, Step 2, and Figure 1, Steps 1 and 2), as in instant claim 2, lines 8-9; claim 3, lines 9-10; and claim 4, lines 11-12.

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33. After the PCR reactions, said reactions are analyzed immediately (continuous) or stored at room temperature for up to 36 hours (time) before fluorescence analysis (discontinuous) (Vogelstein et al., page 9236, column 2, lines Step 1, last two lines), as in instant claims 5-7.

34. Guilfoyle et al. and Vogelstein et al. do not disclose the limitation of claims 13-16.

35. Kato discloses an improvement for isolating coding sequences using molecular indexing (page 394, column 1, lines 1-24). The method of Kato comprises total mRNA (gene expression) population and the use of 3' end cDNAs generated by class II restriction enzymes (Kato, Abstract etc.) wherein said method divides the entire mRNA into 576 subpopulations (Kato, page 395, column 2, 11-15), as in instant claims 13-16.

36. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by the improvement of Vogelstein et al. for PCR reactions cited above to improve the method of Guilfoyle et al. as directed to quantifying PCR products. An artisan of ordinary skill in the art would be further motivated to improve the class II restriction enzyme reaction indexing method of Guilfoyle et al. with the class II restriction enzyme reaction molecular indexing method of Kato for isolating coding sequences. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use an indexing method of indexing as disclosed by Guilfoyle et al., Vogelstein et al., and Kato.

CONCLUSION

37. NO CLAIM IS ALLOWED.

38. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the

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Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 872-9306.

39. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

40. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

41. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

C. Dune Ly
5/17/04

Ardin H. Marschel 5/17/04
ARDIN H. MARSCHEL
PRIMARY EXAMINER